



## Is Procidentia a Distinct Disease? Comparison of Risk Factors

### Procidentia Farklı Bir Hastalık Mıdır? Risk Faktörlerinin Karşılaştırılması

Procidentia

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#### Özet

**Amaç:** Total prolapsus, diğer bir ifadeyle procidentia vajinanın tümünün dışı dönmesi olarak tanımlanır. Yaş, gebelik doğum, pelvik cerrahi öyküsü ve kabızlık, kronik pulmoner hastalıklar, obezite gibi karın içi basıncı artıran durumlar pelvic organ prolapsusu için risk faktörleridir. Bu çalışma anterior, posterior, apikal ve total vaginal duvar prolapsusu insidanslarını, kompartmanlar arası, total ve subtotal prolapsus arasındaki risk faktörleri açısından farklılıkları belirlemektir. **Gereç ve Yöntem:** Bu retrospektif çalışma prolapsus cerrahisi geçiren kadınları kapsar. Total ve subtotal prolapsusu olanlar parite, yaş, vücut kitle indeksi, menapoz ve laboratuvar verileri gibi potansiyel risk faktörleri açısından tek yönlü varyans analizi, Ki kare ve Fisher testi kullanılarak kıyaslandı. **Bulgular:** Prolapsus cerrahisi geçiren 179 kadın arasında 29 kadın total uterovajinal prolapsus olarak değerlendirildi. Subtotal prolapsusu olan kadınlar ( $29.4 \pm 3.7$ ) anlamlı olarak total prolapsusu olanlardan ( $26.1 \pm 3.3$ ) daha şişmandı ( $p < 0.001$ ). Yaş, parite, histerektomi öyküsü ve menapoz durumu açısından fark yoktu. Anterior vajinal duvar defekti olanlarda multipartite oranı diğerlerine kıyasla daha azdı ( $52.4$  vs  $70.5-88.9\%$ ,  $p = 0.03$ ). Tartışma: Biz total uterin veya vajinal kubbe prolapsusun farklı bir durum olduğunu ve yaş ve doğum gibi bilinen risk faktörlerinden farklı bazı spesifik veya belirlenmemiş faktörlerle ilişkili olabileceğini varsayımında bulunuyoruz. Total prolapsusu olan kadınlar daha incedi ve anterior vajinal duvar defektleri multipartite ile daha az ilişkiliydi. Bu bulgular ışığında gelecekte yapılacak çalışmalar ile total uterovajinal prolapsusun patofizyolojisini açıklamayı planlayan çalışmalar yapılmalıdır.

#### Anahtar Kelimeler

Pelvic Organ Prolapsusu; Procidentia; Total Uterovajinal Prolapsus

#### Abstract

**Aim:** Total prolapse—in other words, procidentia—refers to the complete eversion of the total length of the vagina. Age, pregnancy, delivery, previous pelvic surgery, and conditions that increase intra-abdominal pressure, such as chronic pulmonary disease, constipation, and obesity are risk factors for pelvic organ prolapse. This study aims to assess the incidence of anterior, posterior, apical, and total prolapse and to determine differences in the risk factors for different vaginal compartment prolapse, total prolapse, and subtotal prolapse. **Material and Method:** This is a retrospective study of patients who underwent prolapse surgery. Comparison of possible risk factors such as parity, age, body mass index, menopause, and preoperative laboratory results were done between women with total and subtotal uterovaginal prolapse by using one way analysis of variance, chi-square, and Fisher tests. **Results:** A total of 29 women had total uterovaginal prolapse among 179 women who underwent prolapse surgery. Women with subtotal prolapse ( $29.4 \pm 3.7$ ) were significantly more obese than women with total prolapse ( $26.1 \pm 3.3$ ), ( $p < 0.001$ ). Age, parity, hysterectomy history, and menopause status were similar. Multiparity was less in women with dominant anterior vaginal wall defect than in others ( $52.4\%$  vs.  $70.5-88.9\%$ ,  $p = 0.03$ ). **Discussion:** We hypothesized that total uterine or vault prolapse is a different entity that has some specific risk factors other than the primary known risk factors of delivery and age. Women with procidentia were thinner and anterior vaginal wall prolapse was less strongly associated with multiparity. Future studies are needed to understand the pathophysiology of total uterovaginal prolapse.

#### Keywords

Pelvic Organ Prolapse; Procidentia; Total Uterovaginal Prolapse

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## Introduction

Pelvic organ prolapse (POP) is defined as protrusion of one or more of the pelvic organs into the vaginal canal or beyond the vaginal opening. Older terms describing POP such as cystocele, urethrocele, and rectocele have been replaced because they imply an unrealistic certainty about the structures on the other side of the vaginal bulge, particularly in women who have had previous POP surgery. The current practice is to divide the pelvis into anterior, posterior, and middle or apical compartments. The estimated prevalence of POP ranges from 37% to 50% depending on the definition and study population [1, 2]. The lifetime risk of requiring surgery is about 12% by age 80. Furthermore, despite adequate surgical treatment, the risk for reoperation is close to 30% [3, 4].

The severity of POP can be assessed according to the most severe portion of the prolapse after the full extent of the protrusion has been determined. In all measuring or grading systems the extent of prolapse is evaluated relative to the fixed anatomic, hymen, or introitus. The preferred method for describing and documenting the severity of POP is the Pelvic Organ Prolapse Quantification (POP-Q) system. Total prolapse, in other words procidentia, refers to the complete eversion of the total length of the vagina. The distal portion protrudes at least the total vaginal length minus 2 cm beyond the hymen. Total uterine prolapse or vaginal vault prolapse represents failure of all the vaginal supports.

Age, pregnancy, delivery, previous pelvic surgery, and conditions that increase intra-abdominal pressure, such as chronic pulmonary disease, constipation, and obesity are risk factors for POP [5]. There are only a few data about the progression, regression, and natural history of POP. Also, the risk factors specific to prolapse of different compartments or combinations are unknown. In a cross sectional study, 24% of women had no prolapse, 38% had stage I prolapse, 35% had stage II prolapse, and only 2% had stage III prolapse [6]. Annual regression rates were reported as between 22% and 48% in a longitudinal study [6, 7]. Prolapse occurs due to the weakening of endopelvic fascia and loss of vaginal or uterine support such as ligaments. Defects in vaginal supporting tissues may occur in isolation (e.g., anterior vaginal wall only), but they are more commonly combined. In some women, there may be only a single compartment defect, but loss of apical support is common among women with anterior wall prolapse that extends beyond the hymen [7, 8]. Anterior vaginal wall prolapse is the most common form of prolapse [8]. We hypothesized that total uterine or vault prolapse is a different entity that has some specific risk factors other than the primary known risk factors of delivery and age. This study aims to assess the incidence of anterior, posterior, apical, and total prolapse and to determine differences in the risk factors for different vaginal compartment prolapse, total prolapse, and subtotal prolapse.

## Material and Method

This is a retrospective study of patients who underwent prolapse surgery between July 2012 and December 2015 in Bezmialem Vakif University, Istanbul, Turkey. As this is a non-interventional retrospective study, formal ethical approval was not obtained. The demographic data, including age at surgery,

parity, obstetric history, history of operative delivery, smoking, and menopausal status, were all retrieved from the medical records and/or the centralized computer system by the authors. Clinical details such as medical tests and body mass index were recorded. Postmenopausal status was defined as amenorrhea more than one year since the last menstrual period. Body mass index (BMI) was calculated as weight divided by the square of height.

Pelvic anatomical support was assessed while the woman strained maximally in the dorsal lithotomy position using the POP-Q system prior to surgery. Colposuspension or mid-urethral sling procedures were performed in cases of coexisting stress urinary incontinence, which was confirmed with a cough stress test. Obliterative surgery, such as Le-Fort partial colpocleisis or total colpocleisis, corrected POP by closing off the vaginal canal according to the patient's choice and functional status. The vaginal vault was suspended either abdominally (sacrocolpopexy) or transvaginally (uterosacral ligament suspension). Subjects were excluded if they demonstrated the following: stage 0 and stage 1 prolapse, women with POP who did not desire surgical correction of prolapse, prior prolapse surgery, prior incontinence surgery, or any contraindication to surgery. Subjects requiring concurrent surgery for stress urinary incontinence were eligible for the study.

Descriptive statistics were computed and nonparametric statistics were presented for non-normally distributed variables. The one way analysis of variance (ANOVA) was used for the comparison of continuous variables. Chi square test and Fisher's exact tests were used to compare categorical variables. Data were analyzed by using IBM SPSS version 21 for all statistical tests, and differences were considered significant at  $P < 0.05$ .

## Results

During the study period, a total of 188 women with POP underwent surgery for prolapse. Three patients with a history of a previous POP surgery, 2 women with previous colposuspension, and 4 women with incomplete data were excluded. There were remaining 179 women who underwent one of the following operations: colporrhaphy anterior, colporrhaphy anterior, abdominal or vaginal hysterectomy, sacrocolpopexy, uterosacral ligament suspension, or colpocleisis. The mean age was  $59.3 \pm 10.4$  years (range 31–84, 95 % CI=57.7–60.9), with a mean BMI of  $29.3 \pm 3.9$  (range 20.3–37.3, 95 % CI=28.7–29.9). The majority of patients were postmenopausal (140 out of 179; 78.2 %).

A total of 78 (40.2%) patients underwent anterior vaginal wall prolapse surgery (anterior colporrhaphy), whereas 60 (33.5%) patients had a posterior colporrhaphy anterior, and 124 (69.2 %) women had surgery for apical prolapse. Combinations of three compartmental defects were operated on in 61 women. We compared the patient characteristics among groups according to compartment—solely anterior, posterior, apical, or multicompartmental. Demographic data and patient characteristics of patients grouped by anterior, posterior, and apical defect are presented in Table 1. There were no statistically significant differences in known risk factors such as age, parity, gravidity, obesity, and previous hysterectomy. Multiparity, defined as vaginal delivery  $>2$ , was less frequent in women with dominant anterior vaginal wall defect than in others (52.4 vs.

Table 1. Demographic and baseline characteristics of participants with anterior, posterior, apical vaginal wall prolapse and combination of three compartments. BMI: body mass index; SD: standard deviation.

	Anterior (n=21)	Posterior (n=88)	Apex (n=88)	Combined (n=61)	P value
Age, years (mean±SD)	56.7±12.4	57.1±10.1	59.9±9.6	59.5±10.9	0.5
Gravidy (mean±SD)	4±2.8	5.6±2.9	4.5±2.3	5.2±2.3	0.1
Parity (mean±SD)	3.1±1.9	4.1±2.1	3.7±1.9	4±1.9	0.3
Multiparity, N (%)	11 (52.4)	8 (88.9)	62 (70.5)	50 (82)	0.03
BMI	29.4±3.7	30±3.9	28.8±4.2	29.8±3.5	0.4
ABO blood group, N (%)					
A	11(52.4)	4 (44.4)	38(43.2)	27(44.3)	0.7
B	4 (9)	0 (0)	13 (14.8)	13 (21.3)	
O	6 (28.6)	4 (44.4)	32 (36.4)	19 (31.1)	
AB	0 (0)	1 (11.1)	5 (5.7)	2 (3.3)	0.1
Preoperative hematocrit (mean±SD)	39.1±3.7	41.1±1.3	38.2±3.9	38.9±3.1	
Preoperaive platecrit (mean±SD)	0.29±0.06	0.20±0.04	0.27±0.07	0.22±0.07	0.6
Smoking, N (%) *	2 (9.5)	1 (11.1)	12 (13.6)	4(6.6)	
Menopause status, N (%)	15 (71.4)	7 (77.8)	72 (81.8)	46 (75.4)	0.7
History of hernia, N (%)*	2(9.5)	2 (22.2)	3 (3.4)	6 (9.8)	0.1
Previous hyster- ectomy, N (%)*	3 (14.3)	2 (22.2)	5 (5.7)	5 (8.2)	0.2

70.5-88.9%, p=0.03). Distribution of operation sites and operation combinations are shown in Figure 1. Concurrent surgery

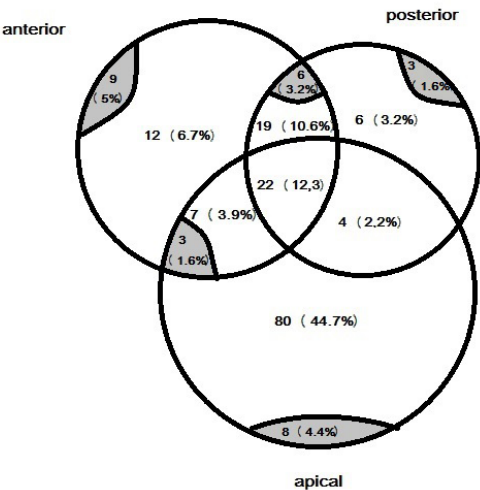


Figure 1. Distribution of cases of pelvic organ prolapse according to anterior, posterior, and apical vaginal wall compartments. Gray areas represent the additional anti-incontinence operations for stress urinary incontinence.

for all three compartments, anterior, posterior, and apical, was performed on 22 (12.3%) women. Concurrent anterior and posterior vaginal wall surgery was the most frequently performed surgery (13.9%), followed by anterior vaginal wall and apical prolapse surgery (5.6%). Twenty nine women (15.3%) had an additional anti-incontinence operation, either colposuspension or a mid-urethral sling. A total of 110 (61.4%) women underwent a hysterectomy, most of them performed transvaginally (95/110; 86.3%).

A total of 29 women had total uterovaginal prolapse and 3 had vaginal cuff prolapse. Comparison of demographic data and patient characteristics between women with total uterovagina prolapse and subtotal prolapsed is shown in Table 2. Women with subtotal prolapse (29.4±3.7) were significantly more obese than women with total prolapse (26.1±3.3), (p<0.001). Age, parity, and other factors were similar. Also, the hysterectomy history rate was similar between women with total and subtotal prolapse.

Table 2. Demographic and baseline characteristics of participants with utero-vaginal prolapse and subtotal uterovaginal prolapse. BMI: body mass index; SD: standard deviation; UVP: Uterovaginal prolapse

	Total UVP N=29	Subtotal UVP N=150	p value
Age, years (mean±SD)	61.2±13.1	58.9±9.8	0.3
Gravidy (mean±SD)	4.2±2.4	4.8±2.2	0.2
Parity (mean±SD)	3.7±1.7	3.8±2	0.2
Multiparity, N (%)	27 (93.1)	144 (96)	0.6
BMI	26.1±3.3	29.4±3.7	<0.001
ABO blood group, N (%)			
A	12 (41.5)	68 (45.4)	0.3
B	3 (10.3)	5 (3.3)	
O	3 (10.3)	27 (18)	
AB	11 (37.9)	50 (33.3)	0.8
Preoperative hematocrit (mean±SD)	38.6±2.9	38.7±3.7	
Preoperaive platecrit (mean±SD)	0.29±0.07	0.27±0.04	0.2
Smoking, N (%) *	2 (6.9)	17 (11.3)	0.7
Menopause status, N (%)	23 (79.3)	118 (83.6)	0.8
History of hernia, N (%)*	3 (10.3)	9 (6)	0.4
Previous hysterectomy, N (%)*	5 (17.2)	10 (6.7)	0.07

Discussion

The behavior and pathophysiology of POP are poorly understood and the available evidence is scarce. The etiologies of POP include aging, pregnancy, mode of delivery, previous hysterectomy, previous POP surgery, conditions that increase intra-abdominal pressure, such as chronic pulmonary disease, constipation, obesity, and instrumental delivery [5, 9]. The etiologies of POP weaken the pelvic floor muscles and ligaments, which support the bladder, urethra, uterus, and rectum. This, in turn, can lead to detachment from the ligaments or pelvic bone where the muscles were attached [10]. The various forms of POP share common risk factors and promoters. We hypothesized that total uterovaginal prolapse is not the progression of a condition caused by common risk factors related to age and pregnancy. Instead, it could be a clinical manifestation of a pre-existing, undiagnosed condition, or a congenital predisposition triggered by common risk factors such as vaginal delivery. If it is the progression of disease it should have linear correlation with age, parity, and birth weight. However, our results showed that except for BMI, risk factors did not significantly differ between total and subtotal prolapse. In this retrospective analysis, multiparity was shown to be significantly associated with posterior, apical, and combined vaginal wall prolapse, but not significantly associated with anterior vaginal wall prolapse, on univariate analysis. Less-severe forms of POP are present not only in women who have given

birth but also in premenopausal nulliparous women in whom the prevalence of POP is similar to that of women who delivered via caesarean section [10]. Caesarean delivery seems to protect against prolapse development whereas instrumental and forceps delivery increases the risk [11, 12]. Our findings were similar to previous reports. According to data of the incidence of POP that restricted by studies of POP surgery, both the incidence and prevalence of POP increase with advancing age. Between the ages of 30 and 80, incidences of POP rise steadily; the peak incidence of such surgery is in individuals aged 60–69 years [4, 13]. However, older age was not found to be associated with more severe prolapse in our study population. To the best of our knowledge this is the first report that evaluates possible risk factors of procidentia.

Larger waist and increasing body mass index was also associated with the risk of developing POP [8, 11]. Obese and overweight women with BMI over 26 kg/m<sup>2</sup> are more likely to have POP and to undergo POP surgery [11]. It could be expected that higher BMI is associated with more-severe stages of prolapse. However, in contrast to these expectations, women with total prolapse in our study sample were thinner. We suggest that procidentia might have other specific risk factors or predisposing factors. POP is associated with reduction in total collagen content and change in distribution of collagen type [14, 15]. In relation to collagen, joint hypermobility and various collagen diseases such as Ehlers-Danlos or Marfan syndrome are linked with POP [16]. All these factors are indicative of the systemic manifestation of collagen abnormalities and suggest a role for congenital predisposition in POP etiology [17, 18]. POP is not a condition caused by pregnancy alone; it could be a clinical manifestation of a preexisting, undiagnosed condition or a congenital predisposition triggered by pregnancy and delivery. POP can affect the apex of the vagina, anterior and posterior vaginal wall, usually in complex interaction and some combinations. Epidemiological studies [19, 20] provide evidence for these complex and interrelated structures of pelvic floor support defects. There is a thought that anterior, posterior, and apical vaginal wall prolapses should be evaluated and operated on in isolation. There are numerous reports on the incidence and degree of prolapse in selected groups, but it is difficult to extrapolate these data to the general population. However, there are only a few reports about incidences of defects of various compartments of the vaginal wall [7, 8]. Cystocele or anterior vaginal wall prolapse was the most common form of prolapse, accounting for more than half [7, 8]. Also, in some women there may be only a single compartment defect, but loss of apical support is common among women with anterior wall prolapse that extends beyond the hymen [10]. In our study population, who consisted of patients undergoing POP surgery, the majority of patients had apical defect; anterior vaginal wall defect was the second most frequent. However, this data should not be extrapolated to the general population.

One of the limitations of this study is its retrospective design, which could create selection bias and reduce the reliability of data regarding gynecological history. Another limitation is the relatively small size of the study population, which represents the single center population data. Our study population was composed of women who were admitted for POP surgery; thus,

this data does not represent the general population or mild forms of POP. The strength of our study is that, to the best of our knowledge, this is the first report that evaluates possible risk factors for total uterovaginal prolapse and for separate prolapse.

In the present study, we evaluated the clinical and basic characteristics of women undergoing POP surgery. We compared the possible risk factors and other properties between women with total uterovaginal prolapse and those with mild forms of prolapse. Women with procidentia were thinner than those with stage 2 or 3 POP. When we compared cases according to the compartment of vaginal support, women with anterior vaginal wall prolapse were less likely to have parity lower than three. Future studies that include a larger number of patients and prospective analytic investigations, along with studies that evaluate the specific predisposing factors for total uterovaginal prolapse surgery, are needed to understand the pathophysiology of this severe disease.

### Competing interests

The authors declare that they have no competing interests.

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